fragment thereof for said enzyme, having a first detectable proximity-sensor peptide incorporated into a first position of said substrate and a second detectable proximity-sensor peptide incorporated into a second position of said substrate, thereby providing a semi-synthetic multiple labeled polypeptide substrate having a first structural conformation in said unmodified state and a second structural conformation in said modified state, said proximity sensors being spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of said structural conformations being indicative of the effect of said enzyme on said substrate.

79. The composition of claim 78, wherein said enzyme a kinase.

80. The composition of claim 79, wherein said kinase is Abelson protein tyrosine kinase.

81. The composition of claim 78, wherein said peptide substrate is Crk-II.

D' cont.

82. The composition of claim 78, wherein said modification of said substrate is a post-translational modification.

83. The composition of claim 82, wherein said modification of said substrate is a phosphorylation modification.

84. The composition of claim 82, wherein said modification of said substrate is a dephosphorylation

modification.

85. The composition of claim 78, further comprising a modulator of said enzyme.

86. The composition of claim 85, wherein said modulator of said enzyme inhibits said enzyme activity.

87. The composition of claim 85, wherein said modulator of said enzyme activates said enzyme activity.

88. The composition of claim 78 wherein said first detectable proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said semi-synthetic multiple labeled polypeptide, the C-terminus of which is peptide bonded to the N-terminus of said second detectable proximity-sensor peptide.

89. The composition of claim 78 wherein said enzyme is a recombinant polypeptide. —new matter

D' cont

90. The composition of claim 78 wherein said first and second detectable proximity-sensor peptides of said semi-synthetic multiple labeled polypeptide comprise a FRET pair.

91. The composition of claim 90 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY fluorescein and BODIPY FL fluorescein, β-phycoerythrin and CY5, and pyrene and coumarin.

92. The composition of claim 90, wherein said FRET pair comprises fluorescein and tetramethylrhodamine.